AMENDMENTS TO THE CLAIMS:

Claims 1-60 are pending. Claims 1-55 are amended herein. Claims 56-60 and added herein. This listing of claims will replace all prior versions, and listings of claims, in the application.

LISTING OF CLAIMS:

1. (Currently amended) A method for predicting a crystal equilibrium condition for biomacromolecule crystallization and for crystallizing a biomacromolecule, comprising:

setting up at least one biomacromolecule solubility experiment, comprising the steps of:

a) preparing a solution of the biomacromolecule in a solvent, the solution having a biomacromolecule ~~concentration,~~ concentration;

b) selecting a variable ~~quantity,~~ quantity;

c) selecting an assembly parameter, being one or more of a surface tension and a surface ~~pressure,~~ pressure;

d) monitoring a response of the assembly parameter while varying the variable quantity in a suitable way so that the response exhibits a ~~transition,~~ transition;

e) obtaining an equilibrium biomacromolecule concentration based on the ~~transition,~~ transition; and

f) defining a crystal equilibrium condition according to which a biomacromolecule crystallization concentration exceeds the equilibrium biomacromolecule concentration,

and crystallizing the biomacromolecule.

2. (Currently amended) The method ~~as claimed in~~ of Claim 1, wherein the solution has further a pH and a temperature, and the variable quantity is one of the biomacromolecule concentration, the pH and the temperature.

3. (Currently amended) The method ~~as claimed in~~ of Claim 2, wherein the solution further comprises an additive, the solution has an additive concentration, and the variable quantity is one of the biomacromolecule concentration, the pH, the temperature and the additive concentration.

4. (Currently amended) The method ~~as claimed in~~ of Claim 1, wherein the solution has a surface.

5. (Currently amended) The method ~~as claimed in~~ of Claim 4, wherein the biomacromolecule is not prone to unfolding at the surface of the solution.

6. (Currently amended) The method ~~as claimed in~~ of Claim 2 ~~or Claim 3~~, wherein the transition is associated with a critical magnitude of the variable quantity.

7. (Currently amended) The method ~~as claimed in~~ of Claim 2 ~~or Claim 3~~, wherein the transition is between a changing response of the assembly parameter and a substantially unchanging response of the assembly parameter.

8. (Currently amended) The method ~~as claimed in~~ of Claim 2 ~~or Claim 3~~, wherein the transition is associated with a critical magnitude of the variable quantity, and further wherein the transition is between a changing response of the assembly parameter and a substantially unchanging response of the assembly parameter.

9. (Currently amended) The method ~~as claimed in~~ of Claim 8, wherein the substantially unchanging response corresponds to a substantially minimal value of the assembly parameter.

10. (Currently amended) The method ~~as claimed in~~ of Claim 8, further defining the crystal equilibrium condition in terms of the critical magnitude, wherein the crystal equilibrium condition prescribes that no crystallization occurs when the variable quantity is smaller than the critical magnitude.

11. (Currently amended) The method ~~as claimed in~~ of Claim 10, wherein the variable quantity is the biomacromolecule concentration, and consequently the equilibrium biomacromolecule concentration equals the critical magnitude.

12. (Currently amended) The method ~~as claimed in~~ of Claim 10, wherein the variable quantity is not the biomacromolecule concentration, and consequently the equilibrium biomacromolecule concentration equals the biomacromolecule concentration.

13. (Currently amended) The method ~~as claimed in~~ of Claim 1, wherein the biomacromolecule to be crystallized is a protein.

14. (Currently amended) The method ~~as claimed in~~ of Claim 13, wherein the protein has a weight less than 200 kDalton.

15. (Currently amended) The method ~~as claimed in~~ of Claim 14, wherein the protein is one of a lysozyme and a concanavalin A.

16. (Currently amended) The method ~~as claimed in~~ <u>of</u> Claim 1, wherein the biomacromolecule to be crystallized is a polypeptide.

17. (Currently amended) The method ~~as claimed in~~ <u>of</u> Claim 1, wherein the biomacromolecule to be crystallized is a nucleic acid.

18. (Currently amended) The method ~~as claimed in~~ <u>of</u> Claim 1, wherein the biomacromolecule to be crystallized is a virus.

19. (Currently amended) The method ~~as claimed in~~ <u>of</u> Claim 1, wherein the biomacromolecule to be crystallized is a virus fragment.

20. (Currently amended) The method ~~as claimed in~~ <u>of</u> Claim 3, wherein the additive is a salt.

21. (Currently amended) The method ~~as claimed in~~ <u>of</u> Claim 3, wherein the additive comprises organic molecules.

22. (Currently amended) The method ~~as claimed in~~ <u>of</u> Claim 3, wherein the additive comprises polymers.

23. (Currently amended) A method for predicting a crystal equilibrium condition for protein crystallization and for crystallizing a protein, comprising<u>:</u>

setting up at least one biomacromolecule solubility experiment, comprising the steps of<u>:</u>

a) preparing a solution of the protein in a solvent, the solution further comprising an additive, the solution having a protein concentration, an additive concentration, a pH and a temperature, the solution having a surface, the surface having a surface tension and a surface pressure, the protein being not prone to unfolding at the ~~surface,~~ <u>surface;</u>

b) defining an assembly parameter to be one of the surface tension and the surface ~~pressure,~~ <u>pressure;</u>

c) selecting a first variable quantity and a second variable quantity from the protein concentration, the additive concentration, the pH and the ~~temperature,~~ <u>temperature;</u>

d) varying the first variable quantity in a suitable way so that the assembly parameter exhibits a transition between a changing response and a substantially unchanging response, wherein the substantially unchanging response corresponds to a first substantially minimal value of the assembly parameter, the transition being associated with a first critical magnitude of the first variable ~~quantity,~~ <u>quantity;</u>

e) varying the second variable quantity in a suitable way so that the assembly parameter exhibits a transition between a changing response and a substantially unchanging response, wherein the substantially unchanging response corresponds to a second substantially minimal value of the assembly parameter, the transition being associated with a second critical magnitude of the second variable ~~quantity,~~ quantity;

f) constructing a solubility curve comprising points, each point being a pair of the first critical magnitude and the second critical magnitude, in order to assist in defining a crystal equilibrium ~~condition,~~ condition; and

g) obtaining an equilibrium protein concentration and defining the crystal equilibrium condition which is based on the solubility curve, and which prescribes that crystallization occurs when the first variable quantity exceeds the first critical magnitude of the pair, and the second variable quantity exceeds the second critical magnitude of the pair,

and crystallizing the protein using a protein crystallization concentration exceeding the equilibrium protein concentration.

24. (Currently amended) The method ~~as claimed in~~ of Claim 23, ~~where~~ wherein in step (c) the protein concentration is one of the first variable quantity and the second variable quantity, and hence in step (g) the equilibrium protein concentration is correspondingly one of the first critical magnitude and the second critical magnitude.

25. (Currently amended) The method ~~as claimed in~~ of Claim 23, ~~where~~ wherein in step(c) the protein concentration is not one of the first variable quantity and the second variable quantity, and hence in step (g) the equilibrium protein concentration is the protein concentration.

26. (Currently amended) The method ~~as claimed in~~ of Claim 23, wherein the protein is one of ~~the~~ a lysozyme and ~~the~~ a concanavalin A and the additive is a salt.

27. (Currently amended) A method for predicting an aggregation boundary condition for biomacromolecule crystallization and for crystallizing a biomacromolecule, comprising:

setting up at least one aggregation boundary condition experiment comprising:

a) preparing a solution of the ~~biomacromolecule,~~ biomacromolecule;

b) selecting a variable ~~quantity,~~ quantity;

c) selecting an assembly parameter being one or more of a surface tension and a surface ~~pressure,~~ pressure;

d) measuring the assembly parameter at different ~~times,~~ times;

e) registering an equilibrium assembly parameter;

f) deriving a crystallization coefficient from the equilibrium assembly parameter, the crystallization coefficient being associated with the variable ~~quantity,~~ quantity; and

g) using an aggregation indicator to define an aggregation boundary condition for the biomacromolecule, the aggregation boundary condition prescribing that an aggregation occurs when the crystallization coefficient associated with the variable quantity is larger than the aggregation indicator,

and crystallizing the biomacromolecule.

28. (Currently amended) A method for predicting an aggregation boundary condition for biomacromolecule crystallization and for crystallizing a biomacromolecule, comprising:

setting up at least one aggregation boundary condition experiment, comprising:

a) preparing a solution of the biomacromolecule in a solvent, the solution having a biomacromolecule concentration and a surface, the surface having a surface ~~pressure,~~ pressure;

b) selecting a variable ~~quantity,~~ quantity;

c) obtaining the surface pressure at different times, while varying the variable ~~quantity,~~ quantity;

d) recording a time dependent equilibrium surface pressure which is associated with the variable ~~quantity,~~ quantity;

e) formulating a time-dependence profile based on the equilibrium surface pressure, which is associated with the variable ~~quantity,~~ quantity;

f) deriving from the time-dependence profile a crystallization coefficient of the biomacromolecule, that is associated with the variable ~~quantity,~~ quantity; and

g) obtaining from the crystallization coefficient an aggregation indicator in order to define an aggregation boundary condition for the biomacromolecule, the aggregation boundary condition prescribing that an aggregation occurs when the crystallization coefficient associated with the variable quantity is larger than the aggregation indicator,

and crystallizing the biomacromolecule.

29. (Currently amended) The method ~~as claimed in~~ of Claim 28, wherein the biomacromolecule is not prone to unfolding at the surface of the solution.

30. (Currently amended) The method ~~as claimed in~~ of Claim 28, wherein the solution further has pH and a temperature.

31. (Currently amended) The method ~~as claimed in~~ of Claim 28, wherein the biomacromolecule concentration is in the range 0.01-1. 2 mg/ml.

32. (Currently amended) The method ~~as claimed in~~ of Claim 28, wherein the solution further comprises an additive and the solution has an additive concentration.

33. (Currently amended) The method ~~as claimed in~~ of Claim 30, wherein the variable quantity is one of the biomacromolecule concentration, the pH and the temperature.

34. (Currently amended) The method ~~as claimed in~~ of Claim 32, wherein the variable quantity is one of the biomacromolecule concentration, the additive concentration, the pH and the temperature.

35. (Currently amended) The method ~~as claimed in~~ of Claim 28, wherein the step of deriving the crystallization coefficient comprises the steps of:

obtaining a diffusion time of the ~~biomacromolecule,~~ biomacromolecule;

obtaining an integration time of the ~~biomacromolecule,~~ biomacromolecule; and

dividing the ~~integation~~ integration time by the diffusion time to obtain the crystallization coefficient of the biomacromolecule, that is associated with the variable quantity.

36. (Currently amended) The method ~~as claimed in~~ of Claim 28 wherein the time-dependence profile is given by $\ln(1-p/p_{eq})$, where ln is the natural logarithm, p is the surface pressure and p_{eq} is an equilibrium surface pressure.

37. (Currently amended) The method ~~as claimed in~~ of Claim 36, where the step of deriving the crystallization coefficient comprises the steps of:

constructing a plot of the time-dependence profile against a ~~time,~~ time;

identifying on the plot of the time-dependence profile a first substantially straight linear segment, a second substantially straight linear segment and a third substantially straight linear segment, where the second substantially straight linear segment is later in the time than the first substantially straight linear segment and the second substantially straight linear segment is later in the time than the third substantially straight linear ~~segment,~~ segment;

equating a diffusion time to an inverse slope of the first substantially straight linear ~~segment,~~ segment;

equating a penetration time to an inverse slope of the second substantially straight linear ~~segment,~~ segment;

equating a rearrangement time to an inverse slope of the third substantially straight linear ~~segment,~~ segment;

adding the penetration time and the rearrangement time to obtain an integration time; and

dividing the integration time by the diffusion time to obtain the crystallization coefficient of the biomacromolecule, that is associated with the variable quantity.

38. (Currently amended) The method ~~as claimed in~~ of Claim 28, wherein the biomacromolecule to be crystallized is a protein.

39. (Currently amended) The method ~~as claimed in~~ of Claim 38, wherein the protein has a weight less than 200 kDalton.

40. (Currently amended) The method ~~as claimed in~~ of Claim 39, wherein the protein is one of a lysozyme and a concanavalin A.

41. (Currently amended) The method ~~as claimed in~~ of Claim 28, wherein the biomacromolecule to be crystallized is a polypeptide.

42. (Currently amended) The method ~~as claimed in~~ of Claim 28 wherein the biomacromolecule to be crystallized is a nucleic acid.

43. (Currently amended) The method ~~as claimed in~~ of Claim 28, wherein the biomacromolecule to be crystallized is a virus.

44. (Currently amended) The method ~~as claimed in~~ of Claim 28, wherein the biomacromolecule to be crystallized is a virus fragment.

45. (Currently amended) The method ~~as claimed in~~ of Claim 32, wherein the additive is a salt.

46. (Currently amended) The method ~~as claimed in~~ of Claim 32, wherein the additive comprises organic molecules.

47. (Currently amended) The method ~~as claimed in~~ of Claim 32, wherein the additive comprises polymers.

48. (Currently amended) The method ~~as claimed in~~ of Claim 28, wherein the aggregation indicator is below 9.

49. (Currently amended) The method ~~as claimed in~~ of Claim 28, wherein the aggregation indicator is below 8.5.

50. (Currently amended) The method ~~as claimed in~~ of Claim 28, wherein the aggregation indicator is in a range from 4 to 9.

51. (Currently amended) The method ~~as claimed in~~ of Claim 28, wherein the aggregation indicator is in a range from 4.5 to 8.5.

52. (Currently amended) A method for predicting an aggregation boundary condition for protein crystallization and for crystallizing a protein, comprising:

setting up at least one aggregation boundary condition experiment, comprising:

a) preparing a solution of the protein in a solvent, a salt, and a suitable buffer, the solution having a salt concentration, a protein concentration in a range 0. 01-1. 2mg/ml, a pH and a temperature, the solution having a surface, the surface having a surface pressure, the protein not being prone to unfolding at the surface of the ~~solution,~~ solution;

b) obtaining the surface pressure at different times, while varying the salt ~~concentration,~~ concentration;

c) recording a time-dependent equilibrium surface pressure, which corresponds with an equilibrium time, and which is associated with the salt ~~concentration,~~ concentration;

d) formulating a time-dependence profile, which is given by $\ln(1-p/p_{eq})$, where ln is the natural logarithm, p is the surface pressure and p_{eq} is an equilibrium surface pressure, and which is associated with the salt ~~concentration,~~ concentration;

e) constructing a plot of the time-dependence profile against a ~~time,~~ ~~time~~;

f) identifying on the plot a first substantially straight linear segment, a second substantially straight linear segment and a third substantially straight linear segment, where the second substantially straight linear segment is later in the time than the first substantially straight linear segment, and the third substantially straight linear segment is later in time than the second substantially straight linear ~~segment,~~ segment;

g) equating a diffusion time to an inverse slope of the first substantially straight linear ~~segment,~~ segment;

h) equating a penetration time to an inverse slope of the second substantially straight linear ~~segment,~~ segment;

i) equating a rearrangement time to an inverse slope of the third substantially straight linear ~~segment,~~ segment;

j) adding the penetration time and the rearrangement time to obtain an integration time;

k) dividing the integration time by the diffusion time to obtain the crystallization coefficient of the protein, that is associated with the salt ~~concentration,~~ concentration;

g) obtaining from the crystallization coefficient an aggregation indicator in order to define an aggregation boundary condition for the protein, the aggregation boundary condition prescribing that an aggregation occurs when the crystallization coefficient associated with the salt concentration is larger than the aggregation indicator, the aggregation indicator being in a range from 4.5 to 8.5.

53. (Currently amended) The method ~~as claimed in~~ of Claim 52, wherein the protein is one of a lysozyme and a concanavalin A.

54. (Currently amended) The biomacromolecule crystallized ~~according to any one of the Claims 1-22 and 28-51~~ by the method of Claim 1.

55. (Currently amended) The protein crystallized ~~according to any one of the Claims 23-26, 52 and 53~~ by the method of Claim 25.

56. (New) The biomacromolecule crystallized by the method of Claim 28.

57. (New) The protein crystallized by the method of Claim 52.

58. (New) The method of Claim 3, wherein the transition is associated with a critical magnitude of the variable quantity.

59. (New) The method of Claim 3, wherein the transition is between a changing response of the assembly parameter and a substantially unchanging response of the assembly parameter.

60. (New) The method of Claim 3, wherein the transition is associated with a critical magnitude of the variable quantity, and further wherein the transition is between a changing response of the assembly parameter and a substantially unchanging response of the assembly parameter.